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(54) Title: TWO-COMPONENT COMPOSITION FOR COSMETIC OR PHARMACEUTICAL USE

(57) Abstract: The present invention relates to a biphasic composition for cosmetic or pharmaceutical use comprising antioxidants and beneficial compounds for the skin, such as moisturizers and immunomodulators. The composition comprises ascorbic acid as the antioxidant compound and ceramides as the selected moisturizing agent and betaglycane as the immunomodulator, presenting a low potential risk for sensitization and having effective antioxidant action, in addition to an outstanding sensitive effect.

Title : TWO-COMPONENT COMPOSITION FOR COSMETIC OR PHARMACEUTICAL USE

Field of the Invention

The present invention relates to an aqueous composition especially improved for cosmetic and pharmaceutical compositions, comprising antioxidant compounds and other beneficial compounds for the skin as moisturizers and immunomodulators.

Prior Art

Cosmetic and pharmaceutical compositions including antioxidants are very well known for improving the skin aspect, e.g., preventing marks from showing on the skin, such as wrinkles, flaccidity, spots, or to treat mild problems such as irritations and other mild diseases.

In this kind of composition, antioxidant compounds are commonly used, such as levogyrous ascorbic acid (LAA), popularly known as "Vitamin C" and proanthocyanidins (OPC) because, among other characteristics, they act against the free radicals which accelerate the aging process and the cellular degeneration.

Said compositions lack, however, the supplying of a substantial improvement in the general quality of the skin, because they normally approach one or another problem singly. In addition, if on the one hand antioxidants bring improvement benefits for the skin or help to the cells health, on the other hand they can cause sensitivities to certain people.

When sensitivities occur, they can be attributed to the nature of certain antioxidants or to the concentrations required to obtain the desired benefits, which can vary from 5 to 10% or even 20% by weight. Lower antioxidants concentrations might not be potentially irritant, however, the effects they produce are below what would be desirable.

Still in that respect, compositions comprising antioxidants derivatives are very used. Only as an example, LAA esters can be used instead ascorbic acid in its molecular form (LAA). This kind of composition gives rise, until nowadays, to a great discussion among scientists, as for its effectiveness.

One fact that reinforces the theory of a better effectiveness of the antioxidants in their original form is the quantity of studies and publications related to the stabilization

of such compounds. Examples of these studies are described in Brazilian patent applications PI 9704418-0 and PI 9704728-7 and in the prior art references mentioned therein, all of them dedicated to the LAA stabilization.

The OPC's, in their turn, are known by those skilled in the art from many already published works. One of these relates to the patent granted in the United States under number US 4,698,360, to Masquelier, Jacque.

In that patent, anti-free radicals effects provided by such compounds are discussed, with therapeutic indications, including by oral, intravenous and topic route.

Compounds exclusively comprising OPC can bring beneficial effects to the user, however, they show a limited action and benefits scope.

In a further evolution, the patent granted in the United States to Lerner, Sheldom under number US 5,470,874 describes compositions comprising as main actives associated OPC's as a mixture to the ascorbic acid in its molecular form and derivatives as the ascorbyl palmitate.

As it can be noted from this last document mentioned, the composition taught therein to obtain a set of benefits for the skin is extremely complex, having always more than ten ingredients.

In addition to the composition complexity, the benefit scope provided by such composition is limited. Although the number of benefits counted is larger than the one described in US 4,698,360, these could bring some disadvantages.

A first disadvantage is a result of the high LAA contents used, always above 10%, sometimes reaching 25%, which cause a greater skin exfoliation and an uncomfortable sensation (burning), sometimes causing a contact allergy or even making the skin more sensitive to inflammations.

In addition, these high contents provide a very acid pH that causes a lower effectiveness in the complexing activity of the preservative included therein, namely EDTA, which leads to a faster degradation of the LAA.

Summarizing, the aggressive condition provided by the combination of compounds disclosed in the above patent becomes damaging also because it is free from any present or associated entity capable of reducing such aggressiveness in such a way to supply a comfortable product for the user.

Therefore, it is an objective of the present invention to provide a biphasic

composition for cosmetic or pharmaceutical use which supplies a wide range of benefits, and while in use, provides to the user a solution of commitment between the expected effectiveness, due to the presence of antioxidants, and the comfort for the user, with superior results when compared with the known compositions as far as improvement of skin quality are concerned.

Summary of the Invention

The present invention relates to a biphasic composition for cosmetic or pharmaceutical use wherein it comprises a first phase which contains an antioxidant compound in an aqueous medium, and a second phase which comprises a moisturizer compound and an immunomodulator, and wherein the proportion of said first to the second phase is from 6:1 to 14:1.

Detailed Description of the Invention

It was surprisingly found by the present inventors that a biphasic composition for cosmetic or pharmaceutical use comprising, at least one antioxidant in a first phase and, in a second phase, at least one moisturizing agent and one immunomodulator, wherein the application proportion between the first and the second phases ranges from 6:1 to 14:1, provides a wide range of benefits and, while in use, provides to the user both effectiveness, in view of the presence of antioxidants, and the comfort for the user, i.e., low potential of irritation, with superior results when compared with compositions known from the prior art as far as improvement of skin quality is concerned.

Antioxidants useful for the present invention should be understood as compounds or mixture of compounds which have properties against the free radicals present in the body, especially in the skin.

Moisturizing agents useful for the present invention are compounds or mixtures of compounds able to restructure the skin barrier.

Immunomodulators are understood as any compound or mixture of compounds able to reinforce the skin immunological system.

According to a preferred embodiment of the present invention, the biphasic composition for cosmetic or pharmaceutical use comprises two different phases, which, due to their nature, can be conveniently packed in only one dispenser. Each phase, however, must be present in sealed compartments within said dispenser, which prevent

contact between the phases prior to the moment of use, when they are simultaneously dispensed from said dispenser, e.g., due to incompatibility between both of them, which could lead to the unstableness or degradation of the compounds as time goes by. An example of this kind of package is described in patent document WO 97/27841.

According to the above embodiment of the invention, the biphasic composition comprises in a first dispenser compartment, a first phase containing an aqueous composition comprising an antioxidant, preferably ascorbic acid, present at a concentration from 1 to 30% and, in a second phase, a moisturizer such as ceramides, from 0,5 to 3,0%, and the sodic betaglycan carboxyl immunomodulator, also known as betaglycane, present in a content from 0,5 to 3,0%, the application proportion between said first and second phases being from 6:1 to 14:1. All percentages set forth above are in weight relative to the total weight of the composition of each phase.

In a preferred embodiment of the present invention, such biphasic composition comprises in a first dispenser compartment, a first phase in which an aqueous composition is present, comprising a plurality of antioxidants such as ascorbic acid, present at a percentage from 1 to 20%, and OPC's present from about 0,001 to 2,2% and, in a second phase, a moisturizer such as ceramides, preferably ceramides contained in a liquid crystal emulsion, also called lamellar ceramide, in a content from 0,5 to 3,0%, associated to the sodic betaglycan carboxyl immunomodulator, also known as betaglycane, present in a content from 0,5 to 3,0%, the application proportion between said first and second phases being from 6:1 to 14:1, preferably, between 12:1 to 8:1. All the percentages mentioned above are in weight relative to the total weight of the composition of each phase.

It was found that the use of compositions as described above improves strength and natural protection of the skin against external aggressions due to the association of the restructuring effect of the skin lipidic barrier by the lamellar ceramides with the reinforcement effect of the skin immunological system provided by the betaglycanes.

In an even more preferred embodiment of the invention, the biphasic composition comprises a first phase in a first dispenser compartment, where an aqueous composition is present comprising a plurality of antioxidants such as the ascorbic acid present at a percentage from 1 to 20%, preferably between 5 and 18%, and OPC's, present from about 0,001 to 2,2%, preferably between 0,01 and 1,7% and,

in a second phase, a moisturizer such as ceramides, preferably ceramides contained in a liquid crystal emulsion, also called lamellar ceramide, in a range from 0,5 to 3,0%, preferably between 1,5 to 2,5%, associated to sodic betaglycan carboxyl the immunomodulator, also known as betaglycane, which is present in a content from 0,5 to 3,0%, preferably between 1,5 to 2,5%, the application proportion between said first and second phases being from 6:1 to 14:1, preferably, between 12:1 to 8:1, and most preferably, around 11:1. All the percentages above mentioned are in weight relative to the total weight of the composition of each phase.

It has been observed that an adequate proportion between the first phase and the second phase is at about 6:1 to 14:1, preferably between 12:1 to 8:1 and, most preferably, around 11:1. The association of the two phases recovers the skin vitality and imparts an improvement of the skin strength and natural protection.

In vitro studies carried out by the inventors showed that the effects obtained with the composition of the invention can be improved when the ascorbic acid is the levogyrous ascorbic acid (LAA), present within a selected concentration range.

Several essays were carried out by the inventors with the objective of determining in which concentration range the levogyrous ascorbic acid (LAA) has antioxidant and pro-oxidant activity and the results showed that LAA pro-oxidant action occurs in a concentration range between 0,005% and 0,01% while the antioxidant action occurs in ranges between 0,0001% and 0,001% and between 1 and 10%. In these essays, it was also observed that at concentrations between 0,1 and 0,4%, preferably around 0,3% of OPC's associated to the LAA in an aqueous medium, the pro-oxidant effect of the LAA present in the percentage range where it acts as pro-oxidant is inhibited. This conclusion derives from the observation that, in this essay, the deoxyribose degradation decreases 78%.

Advantageously, said first phase contains the antioxidants in their molecular stable or original form (without degradation) but their salts and esters could also be used, certainly leading to good results. In this last case where salts, esters or polymerized antioxidants are to be used, it is believed that the separation between the first and the second phase prior to use could, in some particular cases, be unnecessary. In addition, other compounds can be easily added to the above described components without representing much difficulty for those skilled in the art. Just as an

example, such compounds include fragrances, thickeners, and moisteners or other moisturizers.

In another even more advantageous embodiment, the biphasic composition of the invention comprises, in a first phase, at least one antioxidant compound in an aqueous medium, at least one deoxygenating compound, and at least one metallic ions sequestering compound, and at least one oxidation reaction reverting compound.

It has been now surprisingly found by the present inventors that the association of at least one antioxidant compound, in an aqueous medium, with an oxidation reaction reverting agent, without considering the oxidation reaction stechiometry, a deoxygenating agent and a metallic ions sequestering compounds, makes it possible to improve the performance and the synergy of such first phase with the second phase of said biphasic composition, even when using ascorbic acid contents lower than 10%, without impairing the composition performance, as it will be further described in detail.

For the purposes of the present invention, some terms definitions are presented below.

An oxidation reaction reverting compound is any compound or mixture of compounds which shows a oxidation potential greater than the oxidation potential of the antioxidant to be stabilized so that the antioxidant subcompounds that are generated return to the original antioxidant form, that is to say, to its molecular form.

Concerning the deoxygenating compound, it is any compound or mixture of compounds able to diminish the oxygen solubility in a medium containing water and the antioxidant to be stabilized.

The metallic ions sequestering compound is any compound or mixture of compounds that shows a low complexing constant and is effective for capturing and retaining such ions at pH values under 5,0. The sequestering effectiveness comprises its capacity of complexing the metallic ions present in a medium containing water with the antioxidant to be stabilized, whereby minimizing and, preferably, preventing the decomposition catalysis of any antioxidant present in that medium.

The above embodiment of the invention is particularly adequate to obtain the desired stabilization effects and, at the same time, comfort for the user. In addition, it provides stabilization of compositions containing antioxidant compounds such as levogyrous ascorbic acid (LAA), proantocyanidins (OPC), or both, the obtained

stabilization being effective for long periods of time.

According to that embodiment of the invention, wherein LAA is present as antioxidant in a water containing medium, the deoxygenating compound is selected from the glycol group, most preferably among propylene glycol and butilene glycol and mixtures thereof, most preferably propylene glycol.

The metallic ions sequestering compound, in its turn, is selected from the group of ethylenephosphonic acids, its salts and mixtures thereof, or from the group that comprises phosphonates, which include di-, tri-, tetra- and pentavalent acids, their salts and mixtures thereof. More specifically, the compound able to sequester metallic ions can be selected from the group that comprises sodium salt of 1-hidroxyethyliden (1,1 diphosphate) acid, ethylenediaminetetra (methylenephosphonic) acid, sodium salt of ethylenediaminetetra (methylenphosphonic) acid, sodium salt of diethyleneaminepenta (methylenephosphonic) acid, hydroethylidene (1,1 diphosphate) acid and mixtures thereof. Preferably the metallic ions sequestering agent is 1- hidroxyethylidene (1,1 diphosphate) acid commercialized under the name Dequest 2010 and supplied by MONSANTO.

According to another preferred embodiment of the invention, the first phase of the biphasic composition comprises antioxidant compounds in an aqueous solution, which also contains the deoxygenating compound and the metallic ions sequestering agent in a proportion varying from 2500:1 to 50:1. In addition, such first phase further includes LAA oxidation reaction reverting compound in a ratio varying from 2520:1 to 20:1 in relation to the sum of the deoxygenating compound and the sequestering agent mass, and in proportion varying from 1:0,02 to 3000:1, in relation to the oxidant compound mass. An advantage resulting from the invention is the LAA outstanding stability as time goes by. When compared to conventional compositions containing the same kind of reverting agent already known by those skilled in the art, the invention permits the use of reverting compounds in significatively lower quantities, making their use possible in cosmetic and/or pharmaceutical compositions, thus overcoming the prior art disadvantages related to the bad smell aspect and the legal limitations of reverting compound concentration.

Suitable oxidation reaction reverting agents are the ones already known for this purpose and include sulphurated compounds, preferably chosen from the group

composed of sodium dithionite, sodium disulphides, calcium disulphides, potassium disulphides, and even most preferably, Glutathion, as well as mixtures thereof.

In a commercially adequate cosmetic composition containing, for example, LAA as the antioxidant agent, it is usually employed within a range from about 0,01%, to about 30%, preferably from about 0,5% to about 20%, by weight, while the deoxygenating compound is used within a range from about 10% to about 25%, preferably from about 16% to about 19%, and the sequestering agent is used within a range from about 0,01% to about 0,20%, preferably from about 0,10% to about 0,20%, all the percentages in weight, based on the total weight of the composition. The oxidation reverting compound is present in a concentration from about 0,01% to about 0,5%, preferably from about 0,05% to about 0,2%. The amounts of these components will depend, however, on the final objectives of the resulting composition, and they are not restrictive of the invention.

In another embodiment of the invention, a first phase of the invention composition comprises the LAA as described in the two last embodiments and OPC's present in a range of about 0,001 to 2,2%, or even present from about 0,01 to 1,7%, and preferably around 0,3%.

Any of these embodiments for the first phase can be successfully considered together with any one of the second phases described above in proportions from 6:1 to 14:1, preferably between 12:1 to 8:1, and most preferably, around 11:1.

The illustrative examples and tests presented below will better describe the present invention. Nevertheless, the illustrated data and procedures relate merely to some embodiment of the present invention and should not be considered as restrictive of its scope.

Example I:

A biphasic composition has been prepared comprising a first phase and a second phase, which comprise:

First Phase

Ingredient	% mass
Water	About 75
Propylene glycol	18
Methyl paraben	0,2
Propyl paraben	0,1
Glutathion	0,1
1-hydroethylidene (1,1 diphosphate) acid Dequest®	0,15
LAA	from 1 to 30
OPC	0,3
Modified Xantham Gum	1,4

Second Phase

Ingredient	% mass	
Water	76,20	Vehicle
Xantham Gum	0,27	Thickener
Methyl paraben (Nipagin)	0,18	Preservative
Propyl paraben (Nipazol)	0,09	Preservative
Carbomer (Carbopol 141)	0,27	Thickener
Glycerin	9,09	Moistener
Essence	0,54	Fragrance
Lamellar ceramide	2,12	Skin barrier restructuration agent
Sodium Lauril lactilate	9,09	Disperser
Sodium carboxymethyl betaglycan (Betaglycane)	2,13	Stimulating active

The above composition permits the simultaneous application of selected proportions of compounds as defined in the first phase and in the second phase, what brings a surprising synergy, providing a wide range of benefits to the user. Among the beneficial effects of this product, many of which are explained in the further detailed tests, the following properties of the composition on the skin are detected :

- Improves its exuberance;
- assuages the aging marks of skin (wrinkles and flaccidity);
- improves the skin tint, assuaging the spots appearance;
- stimulates and protect the skin immunological system;
- improves and recover the skin lipidic barrier;
- reduces dark circles;
- improves the aspect of varicose legs;
- improves oral affections (aphthae).

The results of the tests showed below prove the perception of several benefits by users, as well as prove the clinical effectiveness of the product.

A panel has been composed, in a blind study, with 45 volunteers evaluated at 4 moments: immediately after the first application; after one week of use; after one fortnight of use, and after 30 days of use of the product. The supplied product had selected proportions of the first phase to the second phase about 11:1 and had the composition described in Example I above. In all the analyzed moments, the product was evaluated by the consumer and by the doctor. The results of this evaluation are described in Tables I and II, respectively, where the expressed percentages represent the amount of users who noticed that the correspondent benefit has indeed occurred.

Table I: Evaluation of the product performance by the consumer

Attributes	After 1st Application (%)	After 7 days (%)	After 15 days (%)	After 30 days (%)
Protection	8,9	86,7	86,7	93,3
Skin lightening	40,0	80,0	91,1	95,5
More exuberance	86,7	95,5	97,8	97,8
Improvement of softness	93,3	95,5	97,8	97,8
Improvement of tensing action	93,3	95,5	95,5	95,5
Moisture improvement	93,3	97,8	97,8	97,8
Improvement of fine lines (fine wrinkles)	15,5	55,5	64,5	68,9
Cared/Nourished	68,9	97,8	97,8	97,8

Table 2: Evaluation of the product performance by the doctor

Attributes	After 1st Application (%)	After 7 days (%)	After 15 days (%)	After 30 days (%)
Skin lightening	13,3	60,0	68,9	68,9
Improvement of softness	95,5	95,5	97,8	97,8
Improvement of tensing action	82,2	93,3	93,3	93,3
Moisture improvement	95,5	97,8	97,8	97,8
Improvement of fine lines	17,8	55,5	62,2	68,9

It was observed that the above mentioned results are achieved firstly due to the selection of the nature of the antioxidant compounds and of the moisturizing agents

associated to immunomodulators, which, when in contact with skin, produce an advantageous synergetic effect. It is worth observing that in the group of users, all of them indistinctly noticed an improvement greater than 93% for seven out of eight benefits evaluated.

In addition, equally important, the proportion of availability of the first and second phases permitted to find a solution of commitment between the effective antioxidant action and the comfort to the user.

CLAIMS

1. Biphasic composition for cosmetic or pharmaceutical use characterized in that it comprises a first phase comprising an antioxidant compound in an aqueous medium and a second phase which comprises a moisturizer compound and an immunomodulator and in that the proportion of said first phase to the second phase is from 6:1 to 14:1.

2. Composition according to claim 1, characterized in that the first phase comprises ascorbic acid as the antioxidant compound present at 1 to 30% by weight, and the second phase comprises 0,5 to 3,0% of ceramides as moisturizer, and 0,5 to 3,0% of an betaglycane immunomodulator, the proportion between said first and second phases being in the range of 6:1 to 14:1.

3. Composition according to claim 1 or 2, characterized in that the first phase comprises ascorbic acid present at 0,0001 to 0,001% by weight, preferably 1 and 10% by weight.

4. Composition according to claim 1, characterized in that the first phase comprises a mixture of antioxidants comprising ascorbic acid, present at 1 to 20%, and OPC's, present at 0,001 to 2,2%, wherein the second phase comprises 0,5 to 3,0% by weight of ceramides as moisturizer, preferably lamellar ceramides, and 0,5 to 3,0% of betaglycane immunomodulator, the proportion of use between said first and second phases being from 6:1 to 14:1, preferably between 12:1 to 8:1.

5. Composition according to claim 4, characterized in that the antioxidant compound of the first phase comprises 1 to 20% of ascorbic acid preferably between 5 and 18% and 0,001 to 2,2% of OPC's, preferably between 0,01 to 1,7%, wherein the second phase comprises 0,5 to 3,0% of lamellar ceramides as moisturizer, preferably between 1,5 and 2,5%, and the immunomodulator is betaglycane present at a range of 0,5 to 3,0%, preferably 1,5 to 2,5%, the proportion between said first and second phases being from 6:1 to 14:1, preferably between 12:1 to 8:1, and most preferably around 11:1.

6. Composition according to any of the previous claims, characterized in that the ascorbic acid is under the levogyrous molecular form, the OPC's are grape seed oligomers present at about 0,1 to 0,4%, preferably around 0,3% wherein said first and

second phases are maintained separated prior to the moment of use.

7. Composition according to claim 6, characterized in that the first phase also includes about 15 to 19% of propylene glycol, about 0,01 to 1% of methyl paraben, about 0,05 to 1% of propyl paraben, from 0,05 to 0,5% of glutathion, from 0,1 to 0,5% of 1-hydroethylidene (1,1 diphosphate) acid Dequest ®, the balance being water in enough quantity to complete 100% of the weight of such phase; wherein the second phase also includes selected xantham gum thickeners, carbomer and its mixtures, present at about 0,3 to 0,7%, selected methyl paraben, prophil paraben preservatives and mixtures thereof, present at 0,09 to 0,27%.

8. Biphasic composition for cosmetic or pharmaceutical use characterized in that it comprises a first phase comprising an antioxidant compound in an aqueous medium, a deoxygenating compound, a metallic ions sequestering compound, and a reaction oxidation reverting compound.

9. Composition according to claim 8, characterized in that the antioxidant compound is selected from the group comprising levogyrous ascorbic acid (LAA) and proanthocyanidins (OPC's).

10. Composition according to any of claims 8 and 9, characterized in that the antioxidant is the LAA.

11. Composition according to any one of claims 8 to 10, characterized in that the antioxidant further comprises proanthocyanidins (OPC's).

12. Composition according to any one of claims 8 to 11, characterized in that the deoxygenating compound is a glycol.

13. Composition according to claim 12, characterized in that the deoxigenatyng compound is chosen from propylene glycol, butilene glycol, and mixtures thereof, most preferably the propylene glycol.

14. Composition according to any one of claims 8 to 13, characterized in that the metallic ions sequestering compound is selected from the group comprising ethylenephosphonic acids, their salts and mixtures thereof, or from the group that comprises phosphonates which include di-, tri, tetra- and pentavalent acids, their salts and mixtures thereof.

15. Composition according to claim 14, characterized in that the metallic ions sequestering compound is selected from the group which comprises sodium salt of 1-

hidroxyethyliden (1,1 diphosphate) acid, ethylenediaminetetra (methylenephosphonic) acid, sodium salt of ethylenediaminetetra (methylenphosphonic) acid, diethyleneaminepenta (methylenphosphonic) acid, socium sald of diethyleneaminepenta (methylenephosphonic) acid, hydroethyliden (1,1 diphosphate) acid and mixtures thereof.

16. Composition according to claim 15, characterized in that the metallic ions sequestering compound is 1-hidroxyethyliden (1,1 diphosphate) acid.

17. Composition according to claim any one of claims 8 to 16, characterized in that the oxidation reaction reverting compound is selected from the group comprising sodium dithionite, sodium disulphides, calcium disulphides, potassium disulphides and Glutathion, as well as mixtures thereof.

18. Composition according to claim 17, characterized in that the oxidation reaction reverting compound is Glutathion or sodium dithionite.

19. Composition according to claim any one of claims 8 to 18, characterized in that the composition comprises the deoxigenating compound within a range from about 10% to about 25%, the metallic ions sequestering within a range from about 0,01% to about 0,20%, oxidation reaction reverting compound in a concentration from about 0,01% to about 0,5%, the antioxidant compound content being from about 0,01% to about 30%, all the percentages being expressed by weight, based on the total weight of the composition.

20. Composition according to claim 19, characterized in that it comprises the deoxygenating compound within a range from about 16% to about 19%, the metallic ions sequestering compound within a range from about 0,10% to about 0,20% and oxidation reaction reverter compound at a concentration from about 0,05% to about 0,2%, the antioxidant compound content being from about 0,5% to about 20% by weight.

21. Composition according to claim any one of claims 8 to 20, characterized in that the second phase comprises from 0,5 to 0,3%, most preferably, from 1,5 to 2,5% of moisturizing agents, preferably ceramides, more preferably, lamellar ceramides,; 0,5 to 3,0% and, most preferably, from 1,5 to 2,5% of immunomodulators, preferably betaglycanes, the proportion between the first and the second phases being 6:1 to 14:1, preferably from 8:1 to 12:1, and most preferably, about 11:1.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/00 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 804 168 A (MURAD HOWARD) 8 September 1998 (1998-09-08) column 3, line 30-64 column 4, line 10-12 column 5, line 39-45 column 13, line 26-63 column 15, line 55 -column 16, line 23 claim 1 -/--	1,3,8, 12,13

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 December 2000	18/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bazzanini, R

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/BR 00/00077

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08) page 6, line 3-26 page 8, line 10-17 page 10, line 9-14 page 14, line 30 -page 15, line 10 examples 5,6,11,12 page 31, line 13-25 page 32, line 12-18 claims 1-5	1,3,8, 11-13
X	US 5 902 591 A (HERSTEIN MORRIS) 11 May 1999 (1999-05-11) column 2, line 66 -column 3, line 6 column 3, line 15-23 column 4, line 40-46 column 6, line 54-67 column 7, line 48-50 column 11, line 65 -column 13, line 11	1,3,8,12
A	US 5 626 883 A (PAUL STEPHEN M) 6 May 1997 (1997-05-06) column 2, line 50 -column 3, line 10 column 5, line 55-58 column 7, line 61-67 column 8, line 20-23	1-21
A	US 5 094 783 A (BROUILLETTE WAYNE J ET AL) 10 March 1992 (1992-03-10) column 1, line 56-60 column 2, line 60-63	1-21

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 1,3,6,8-21 have been searched incompletely.

Present claims 1,3,6,8-21 relate to an extremely large number of possible compounds due to the use of very generic words such as "biphasic", "antioxidant", "moisturizer", "immunomodulator" (claim 1) and "deoxygenating compound" (claim 8). Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds specifically mentioned in the description and in the claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/ 00/00077

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